REMARKS

This paper is being filed in response to the Final Office Action dated April 1, 2004. Applicants respectfully request reconsideration of the above-identified application in light of the remarks presented herein.

Claims 44-48, 65-69, 121, and 133 are pending. Claim 67 and 68 have been withdrawn. Therefore, claims 44-48, 65, 66, 69, 121, and 133 are under consideration.

Rejection Under 35 U.S.C. § 103(a)

The Examiner has rejected claims 44-48, 65, 66, 69, 121, and 131 under 35 U.S.C. § 103(a) as being unpatentable over US 5,817,343 (Burke) in view of Kim et al. and Kellerman et al. The Examiner alleges that Burke teaches a method for providing an artificial gradient *in vivo* comprising administering an ethylene-vinyl-acetate device subcutaneously, said device comprising a chemotactic factor such as a chemokine, wherein the administration is useful for the controlled or sustained release of drugs. The Examiner alleges that the difference between Burke and the claimed invention is the absence of the disclosure of MIP-3β and the entrapment of antigen presenting cells.

The Examiner indicates that Kim et al. allegedly teach that MIP-3β is a strong chemoattractant for T cells and mature B cells. The Examiner further alleges that Kellerman et al. teach that MIP-3β is a strong chemoattractant for dendritic cells (DC) and that the colocalization of T cells and DCs is required for efficient initiation of T cell-dependent immunity. In addition, the Examiner alleges that it would have been *prima facie* obvious to one

of ordinary skill in the art at the time of the invention to provide an artificial chemotactic gradient *in vivo* comprising administering an ethylene-vinyl-ethylene device subcutaneously, said device comprising a chemotactic factor, said factor comprising a chemokine as taught by Burke and substituting the specific chemokine MIP-3β as taught by Kim et al. The Examiner contends that one of skill in the art would have been motivated to use the specific chemokine because MIP-3β is a strong chemoattractant for T cells and DCs and thus would prove useful in a controlled or sustained release device used in the treatment of any disease for which the efficient initiation of T cell-dependent immunity, because the device would cause the colocalization of both T cells and DCs. Applicants respectfully disagree.

The present invention relates to a method of providing an artificial chemotactic factor gradient created *in vivo*, which can be used to transiently entrap antigen presenting cells circulating through a subject's bloodstream. Once the antigen presenting cells are entrapped, they can be manipulated *in situ* for therapeutic purposes. For example, these cells can be loaded with one or more immunoregulatory molecules, such as a tumor-associated or infectious disease-associated antigen.

In contrast to the present invention, Burke does not disclose a method for providing an artificial chemotactic factor **gradient** *in vivo* comprising administering a composition comprising one or more chemotactic factor(s), wherein transient entrapment of antigen presenting cells is achieved. Contrary to the Examiner's allegations, Burke merely provides a method of formulating slow release particles for drug delivery comprising forming a polymer solution/drug mixture in a solvent, removing the solvent from the mixture to form a

solid matrix, and fragmenting the matrix at a temperature below the glass transition temperature of the matrix. The focus of Burke is on delivery and stability of labile drugs, **not** on the creation of an artificial chemotactic factor gradient in a subject. Therefore, Burke fails to teach or provide any suggestion or motivation to create an artificial chemotactic factor gradient as in the present invention. Furthermore, there is no guidance provided on the application of a chemotactic factor for the purpose of creating an *in situ* artificial chemotactic factor gradient. Lastly, Burke does not disclose a means for the transient entrapment of antigen presenting cells.

Kim et al. does not cure the deficiency of Burke, since it does not teach an artificial chemotactic factor gradient *in vivo* comprising administering a composition comprising one or more chemotactic factor(s), wherein transient entrapment of antigen presenting cells is achieved. Kim et al. merely discloses the pharmacological activity of MIP-3β to attract T and B cells. There is no mention of the creation of an artificial chemotactic factor gradient nor a suggestion that antigen presenting cells can be transiently entrapped, as in the present invention.

Kellernan et al. also fails to teach an artificial chemotactic factor gradient *in vivo* comprising administering a composition comprising one or more chemotactic factor(s), wherein transient entrapment of antigen presenting cells is achieved. Kellernan et al. teach that MIP-3β and CC chemokine receptor-7 (CCR7) ligands (6Ckine) are potent chemoattractants for dendritic cells. There is no mention of the creation of an artificial chemotactic factor gradient nor a suggestion of the transient entrapment of antigen presenting cells.

None of the references teach or suggest, alone or in combination, all the required limitations of claim 44, i.e. a method for providing an artificial chemotactic factor gradient *in*

vivo comprising administering a composition comprising one or more chemotactic factor(s), wherein transient entrapment of antigen presenting cells is achieved. In particular, none of the references teach or suggest a method for providing an *artificial* chemotactic factor gradient *in vivo*, as claimed.

Applicants also assert that there is no suggestion or motivation to combine the cited references to produce the presently claimed method. Burke, the primary reference, is silent on the creation of an artificial chemotactic factor gradient, the use of chemotactic factors, or transient entrapment of antigen presenting cells. In the absence of such motivation from Burke, one of skill in the art would not be motivated to look to either Kim et al. or Kellernan et al. for guidance on providing the artificial chemotactic factor gradient. Therefore, there is no reasonable expectation of success.

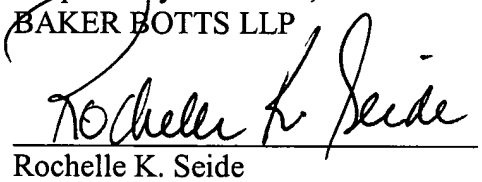
For the foregoing reasons, Applicants respectfully request the withdrawal of the rejection of claims 44-48, 65, 66, 69, 121, and 131 under 35 U.S.C. § 103 (a).

CONCLUSION

Based on the foregoing amendments and remarks, Applicants submit that the present application is in condition for allowance. A Notice of Allowance is respectfully requested.

Applicants request a one month extension of time and enclose herewith the requisite fee as set forth in 37 C.F.R. § 1.17(a)(1). Applicants do not believe that any additional fee is required in connection with the submission of this document. However, should any fee be required, or if any overpayment has been made, the Commissioner is hereby authorized to charge any fees, or credit any overpayments made, to Deposit Account 02-4377. A duplicate copy of this sheet is enclosed.

Respectfully submitted,
BAKER BOTTS LLP



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